

Antioxidant Activity of Adamantylphenols

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Abstract—Antioxidant properties of phenols with *ortho*- and *para*-adamantyl substituents are studied by microcalorimetry using cumene oxidation as a model reaction. The experimental rate constants for inhibition by adamantylphenols (k_7) are comparable to the corresponding values for sterically hindered phenols, and the stoichiometric inhibition coefficient is higher than the calculated one. Adamantylphenols with adamantyl and methyl or methylene bridge groups in the *ortho* positions with respect to the functional group exhibit the maximal activity. The inhibition rate constant takes a maximal value of $k_7 = 3.3 \times 10^4 \text{ l mol}^{-1} \text{ s}^{-1}$ for 2,4-di-(adamantyl-1)-6-methylphenol and a minimal value of $k_7 = 1.4 \times 10^3 \text{ l mol}^{-1} \text{ s}^{-1}$ for 2,4,6-triadamantylphenol. The difference in the rate constants is due to steric hindrances in the reaction of a peroxy radical with the functional group of a phenol surrounded by bulky adamantyl groups.

INTRODUCTION

Sterically hindered phenols are widely used as antioxidants in petroleum and food industry to stabilize fuels, oil, cosmetics, foodstuffs, etc. The extensive application of these antioxidants is due to both their high efficiency and the low toxicity of the products of their conversion.

The reactivity of an antioxidant is largely determined by two factors: (i) the electron-donor (electron-acceptor) nature of the *para* substituents and (ii) the size of the *ortho* substituents. An increase in the size of the *ortho* substituents causes a decrease in the O–H bond strength, thus improving phenol reactivity, and also leads to more pronounced steric hindrances in the reaction of the peroxy radical with the functional center. It has been established that phenols containing at least one *n*- or *sec*-alkyl substituent [1] show the highest activity. Therefore, phenols with *tert*-butyl *ortho* substituents are currently most widely used.

In this work, we studied the antioxidant activity of phenols with the *ortho*- and *para*-adamantyl substituents. Adamantane ($\text{C}_{10}\text{H}_{16}$) is a polycyclic low-strain rigid compound with high symmetry and molecular volume. Adamantyl-containing phenols should exhibit a high thermal stability because adamantane itself is thermally stable up to 660°C. Moreover, some adamantylphenols are bioactive [2, 3]. In this connection, the synthesis and investigation of the properties of such phenols are of theoretical and practical interest.

EXPERIMENTAL

Synthesis and Physical and Chemical Properties of Adamantylphenols

4-(Adamantyl-1)phenol (**I**) was synthesized as described in [4]; b.p., 182–183°C.

2,4-Di-(adamantyl-1)phenol (**II**) was synthesized as described in [5]; b.p., 303–304°C; ^1H NMR spectrum (CD_2Cl_2 , δ , ppm): 1.9 (12H), 2.3 (6H), 2.26 (12H), 4.78 (1H, OH), 6.76 (1H, H_6), 7.18 (1H, H_5), and 7.38 (1H, H_3).

2,4-Di-(adamantyl-1)-6-methylphenol (**III**) was synthesized according to the same procedure as 2,6-di-(adamantyl-1)-4-methylphenol [6]; b.p., 245–247°C; ^1H NMR spectrum (C_6D_6 , δ , ppm): 1.88–2.44 (3OH), 2.07 (3H, CH_3), 7.05 (1H, H_5), and 7.41 (1H, H_3). According to the elemental analysis data, the empirical formula is $\text{C}_{27}\text{H}_{36}\text{O}$.

2,4,6-Tri-(adamantyl-1)phenol (**IV**) was synthesized as described in [5]; b.p., 364–365°C; ^1H NMR spectrum (CDCl_3 , δ , ppm): 1.76 (18H, 9 CH_2), 1.90 (6H, 3 CH_2), 2.14 (21H, 9CH, and 6 CH_2), 5.22 (1H, OH), and 7.12 (2H, H_3 , and H_5).

3,5-Di-(adamantyl-1)pyrocatechol (**V**) was synthesized as described in [7]; b.p., 192–193°C or 194°C [7]; ^1H NMR spectrum (CDCl_3 , δ , ppm): 1.74 (18H, 9 CH_2), 2.04 (12H, 6CH, and 3 CH_2), and 6.72 and 6.83 (2H, H_4 , H, and H_6 , arom.); $J_{46} = 2.2 \text{ Hz}$.

Bis[2-hydroxy-3-(adamantyl-1)-5-methylphenyl]methane (**VI**) was synthesized according to the same procedure as its *tert*-butyl derivative [8]; yield, 75%; b.p., 230–232°C; ^1H NMR spectrum (CDCl_3 , δ , ppm): 1.76 (6H, 3 CH_2 - β), 2.08 (9H, 3CH, and 3 CH_2 - δ), 2.24 (3H, CH_3), 3.84 (2H, bridge CH_2), 5.80 (2H, OH), and 6.92 (4H, H_4 , H_6 , H_4' , and H_6'). According to the elemental analysis data, the empirical formula is $\text{C}_{35}\text{H}_{44}\text{O}_2$.

2,6-Di-(adamantyl-1)-4-methylphenol (**VII**) was synthesized as described in [6]; b.p., 262–263°C or 261–263°C [7]; ^1H NMR spectrum (CDCl_3 , δ , ppm): 1.74 (12H, 6 CH_2), 2.10 (18H, 6 CH_2 , and 6CH),

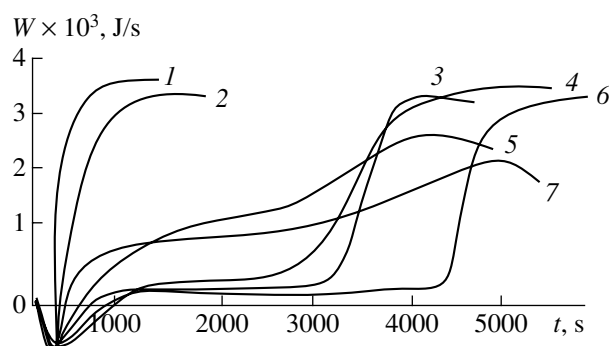


Fig. 1. Heat liberation during cumene oxidation in the presence of adamantylphenols: (1) without inhibitor; (2) 3,5-di-(adamantyl-1)pyrocatechol, $C = 8.22 \times 10^{-4}$ mol/l; (3) 2,4-di-(adamantyl-1)phenol, $C = 1.9 \times 10^{-4}$ mol/l; (4) bis[2-hydroxy-3-(adamantyl-1)-5-methylphenyl]methane, $C = 1.17 \times 10^{-3}$ mol/l; (5) 2,4,6-tri(adamantyl-1)phenol, $C = 1.95 \times 10^{-4}$ mol/l; (6) 2,4-di-(adamantyl-1)-6-methylphenol, $C = 3.01 \times 10^{-4}$ mol/l; and (7) 4-(adamantyl-1)phenol, $C = 1.53 \times 10^{-4}$ mol/l. Initiator, AIBN; $w_1 = 1.2 \times 10^{-7}$ mol l $^{-1}$ s $^{-1}$; $T = 60^\circ\text{C}$.

2.25 (3H, CH₃), 5.3 (1H, OH), and 6.95 (2H, H₃, and H₅).

Determination of the Inhibition Rate Constants

Experiments were carried out on an MKDP-2 differential microcalorimeter designed and constructed at the Institute of Petrochemistry of the Siberian Division of the Russian Academy of Sciences (Tomsk) [9]. Microcalorimetry allows one to determine the rate constant k_7 for the reaction between cumylperoxy radicals and adamantylphenols by measuring the heat of cumene oxidation by oxygen used as a model reaction. The experimental procedure, the cell design, and the detailed derivation of an equation relating the enthalpy of the model reaction and the rate constants for the propagation of radical reactions and their termination on inhibitors are given in [10–13]. The inhibition rate constants for several well-known inhibitors (ionol, hydroquinone, irganox 1010, α -naphthol, and product 2246) [10] agree well with data obtained by alternative methods. The k_2 value was taken in accordance with [14].

The equation for the intensity of heat liberation (W_t) at time t during radical oxidation in the presence of the inhibitor is

$$W_t = \Delta H V \frac{k_2}{k_7} [\text{RH}] \frac{1}{\tau - t},$$

where ΔH is the enthalpy of cumene oxidation, J/mol; V is the volume of the reaction medium, l; $[\text{RH}]$ is the concentration of oxidized cumene, mol/l; k_2 is the rate constant for chain propagation via reaction (I), l mol $^{-1}$ s $^{-1}$; k_7 is the rate constant for chain termination on the inhibitor, l mol $^{-1}$ s $^{-1}$; and τ is the induction period, s.

The inhibition rate constant sought in the study corresponds to the reaction between a peroxy radical and adamantylphenol (reaction (II)):



Figure 1 presents the curves illustrating heat liberation during cumene oxidation in the presence of adamantylphenols. The induction period is observed in the presence of a strong inhibitor. The height of the curve at every time instant is determined by the heat liberation in oxidation (I), which vanishes upon the complete suppression of oxidation. The results of our calculations suggest that the chain length for phenol **IV** (the number of radical regenerations since initiation to termination) is $v \approx 1.20$, whereas, for phenol **III** $v \approx 1.23$ (after 2000 s from the onset of the reaction).

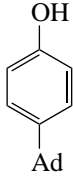


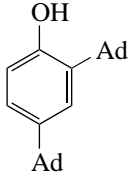
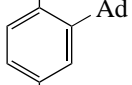
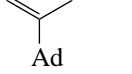
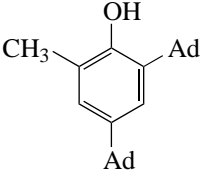
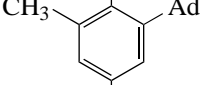
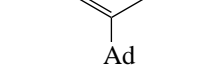
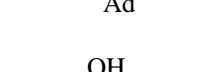
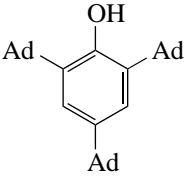
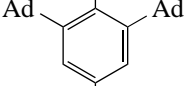
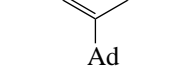
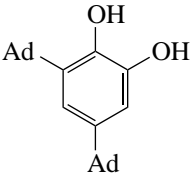
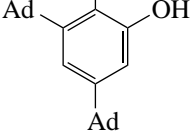
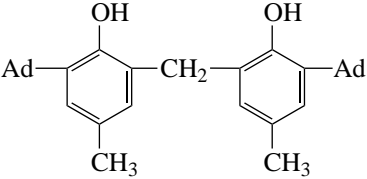
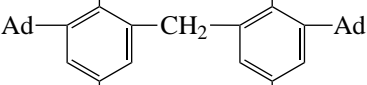

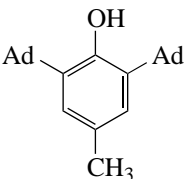
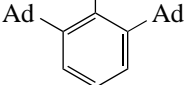
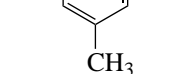
RESULTS AND DISCUSSION

Our experimental results are summarized in the table. The rate constants for the reaction of peroxy radicals with adamantylphenols are lower than those for the relevant reactions involving *tert*-butylphenols. For example, the rate constants for the reactions involving phenol **IV** and inhibitor P-23 containing *tert*-butyl groups instead of the adamantyl groups in positions 2, 3, and 6 are 1.35×10^3 and 2.12×10^4 l mol $^{-1}$ s $^{-1}$, respectively [15]. The maximal k_7 values are observed for phenols **III** and **VI** (see table) containing the adamantyl substituent to one side of the OH group and the methyl group or methylene bridge connecting two aromatic rings on the other. In this case, the k_7 value is higher because of the less substantial steric hindrances. Therefore, adamantylphenols, like phenol **VI**, with spatially separated adamantyl groups can be used as antioxidants.

The structure of **VI** is similar to that of Product 2246 but it has adamantyl instead of *tert*-butyl groups. For these compounds, the curve of heat liberation exhibits two inhibition steps because the functional groups are not equivalent due to hydrogen bonding: inhibition first involves the hydrogen atom that does not form a hydrogen bond and then the less reactive bound hydrogen atom. The rate constants are (l mol $^{-1}$ s $^{-1}$): 39.8×10^5 and 7.7×10^3 for Product 2246 [15] and 1.4×10^4 and 4.4×10^3 for phenol **VI**.

Using the experimental curves shown in Fig. 1, one can qualitatively estimate the inhibitor efficiency: the lower the intensity of heat liberation during the induction period, the more efficient the retardation of the radical reaction by adamantylphenol. Inhibitor **V** causes a dramatic decrease in the oxidation rate. This effect on cumene oxidation is usually observed in the case of alkyl radical acceptors. Therefore, we studied whether or not compound **V** can inhibit styrene polymerization in a vacuum (Fig. 2) and found that the induction period

Rate constants for inhibition by adamantylphenols measured for the model reaction of cumene oxidation. Initiator, AIBN; $w_i = 1.2 \times 10^{-7} \text{ mol l}^{-1} \text{ s}^{-1}$ (the values when $w_i = 6.8 \times 10^{-8} \text{ mol l}^{-1} \text{ s}^{-1}$ are marked with asterisks); $T = 60^\circ\text{C}$

No.	Compound	Formula	$C \times 10^{-4}, \text{ mol/l}$	$W_{\text{st}} \times 10^3, *$ J/s	$\tau, \text{ s}$	f_n^{**}	$k_7 \times 10^{-3}, \text{ l mol}^{-1} \text{ s}^{-1}$
I	4-(Adamantyl-1)phenol		0.76	3.85	3300	4.8	1.75 ± 0.4
			1.53	3.21	5000	3.6	
			3.06	2.57	8600	3.1	
II	2,4-di-(adamantyl-1)phenol		0.95	5.06	2300	2.7	4.5 ± 0.4
			1.9	4.95	3800	2.2	
			3.81	4.68	7800	2.3	
III	2,4-di-(adamantyl-1)-6-methylphenol		0.75	5.17	1500	2.1	38.3 ± 8.3
			1.5	5.32	2500	1.8	
			2.2	5.10	3700	1.9	
			3.01	4.71	5000	1.8	
IV	2,4,6-tri(adamantyl-1)phenol		1.95	4.18	4200	2.4	1.35 ± 0.25
			3.89	3.43	7500	2.1	
			7.78	2.60	12100	1.7	
V	3,5-di-(adamantyl-1)pyrocatechol		4.11	4.74	—	—	—
			8.22	4.49	—	—	
VI	Bis[2-hydroxy-3-(adamantyl-1)-5-methylphenyl]methane		0.88	4.86	3100	3.8	14.6 ± 2.8
			1.17	4.77	4100	3.9	
			1.75	5.21	6100	3.8	
VII	2,6-di-(adamantyl-1)-4-methylphenol		0.18	6.15	1000***	3.7	3.50 ± 0.41
			0.25	6.37	1300***	3.5	
			1.02	6.26	4000***	2.7	

* W_{st} is the intensity of heat liberation during steady-state oxidation (without chain termination on an inhibitor).

** f_n is the number of radical chains terminated by one inhibitor molecule.

*** $w_i = 6.8 \times 10^{-8} \text{ mol l}^{-1} \text{ s}^{-1}$.

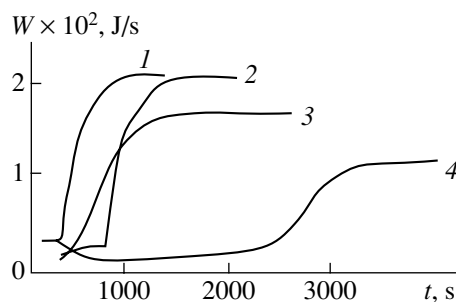


Fig. 2. Heat liberation during styrene polymerization in a vacuum in the presence of the inhibitors: (1) without inhibitor; (2) 2,4,6-tri(adamantyl-1)phenol, $C = 3.3 \times 10^{-3}$ mol/l; (3, 4) 3,5-di(adamantyl-1)pyrocatechol, $C = 7.9 \times 10^{-4} = 1.6 \times 10^{-3}$ mol/l, respectively. Initiator, AIBN; $w_i = 1.2 \times 10^{-7}$ mol l $^{-1}$ s $^{-1}$; $T = 60^\circ\text{C}$.

was observed at a rather high concentration of phenol V. This fact indicates that 3,5-di(adamantyl-1)pyrocatechol cannot efficiently inhibit polymerization and its efficiency is lower than those of benzoquinone and stable nitroxyl phenols.

Taking into account that the peroxy radical is a strong oxidant, reactions can occur that involve both the phenol and adamantane group of the inhibitor. This is also confirmed by the fact that adamantane itself is more reactive during oxidation than cumene [16]. Obviously, the oxidation of the ternary hydrocarbon in adamantane to form intermediate inhibiting centers (phenol or quinoid) occurs via the scheme given in [17].

This explains the high stoichiometric inhibition coefficient for adamantylphenols, but additional studies should be performed to obtain direct evidence.

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